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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,371	04/08/2002	Gregor Cevc	2200437.120US1/VOS-020	1865

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EXAMINER	
HISSONG, BRUCE D	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
10/10/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/890,371	CEVC ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-63 and 65-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-63 and 65-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/8/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/2/2007 has been entered.

2. In the response received on 7/2/2007, the Applicants cancelled claims 64 and 104. Accordingly, all rejections of these claims are rendered moot.

3. Claims 54-63 and 65-103 are currently pending and are the subject of this office action.

Information Disclosure Statement

The information disclosure statement received on 8/8/2007 has been considered by the Examiner.

Specification

1. Objection to the specification, regarding improperly labeled trademarks, is *withdrawn* in response to Applicants deletion of the trademarks ARLACEL and SPAN from the specification, and Applicants arguments that the specification describes the composition of Transfersulin in both general terms and specifically in regards to the chemical composition.

2. The specification is objected to for the following informalities: the specification, on page 27, first paragraph, contains sections of text that have been rendered unreadable.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection maintained

Claims 54-63 and 65-103 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of enablement for a method of transnasally administering a composition comprising a penetrant comprised of any two substances other than a surfactant and a lipid, as set forth on page 4 of the office action mailed on 1/29/2007, and originally set forth on pages 4-5 of the office action mailed on 7/26/2006.

In the response received on 7/2/2007, the Applicants amended the claims to read on a method of transnasally administering a composition comprising a penetrant comprising of any two substances....."wherein the less soluble substance is a lipid and the more soluble substance is a surfactant or more soluble form of the lipid". The Applicants assert that the specification is fully enabling for the claims as currently amended.

These arguments have been fully considered and are not persuasive. Although the amendments to the claims to specifically recite a penetrant comprising a less soluble substance that is a lipid and a more soluble substance that is a surfactant or a more soluble form of the lipid has narrowed the breadth of the claims, the specification has not adequately taught which lipids and/or surfactants which appropriately differ in solubility are suitable for use in the claimed method. In the Applicant's response to the rejection under 35 U.S.C. 103, received on 7/2/2007, the Applicants argue that compositions comprising the lipid didecanoyl-L-alpha-phosphatidylcholine would not be expected "to form a carrier with a penetrant including layers and aggregates with diameter as claimed (and is expected to instead self-assemble into small aggregates in micellar form)". The Applicants also assert that didecanoyl-L-alpha-phosphatidylcholine used with a surfactant such as Tween 80 "would be unlikely to form a penetrant composition having layers and aggregates with diameter as claimed (and instead would likely form micelles)" (see 7/2/2007 response, page 15).

The specification provides a listing of exemplary lipids and surfactants that can comprise the claimed penetrant of the instant method (see pages 26-28). Specifically, phosphatidylcholines (page 27, line 10) are disclosed as useful. However, the Applicants state that the phosphatidylcholine of the cited art would not be expected to act in a manner as to meet the claim limitations, this raises the issue as to how one of ordinary skill in the art would be able to predict whether a given lipid and/or surfactant would meet these claim limitations. The specification does not provide guidance or examples of any lipids, such as phosphatidylcholines, that are not suitable for use in the claimed penetrant. Thus, one of ordinary skill in the art would not be able to predict which of the many possible lipids and surfactants could be used in

the claimed method, and therefore one of ordinary skill in the art could not make and then use the claimed penetrant compositions in methods of transnasal administration, wherein said penetrants comprise any lipid and any surfactant. As Applicants have argued in response to the rejection under 35 USC 103, not all lipids are suitable for use and the specification does not teach how to predict if a given surfactant is suitable. Owing to this unpredictability, a person of ordinary skill in the art would therefore require further, undue experimentation in order to determine which of the many possible lipids and surfactant combinations would produce a penetrant suitable for use in the claimed method of transnasal administration.

Claim Rejections - 35 USC § 112, first paragraph – written description

Rejection withdrawn

Rejection of claim 60 under 35 USC § 112, first paragraph, regarding lack of written description for derivatives and analogs of an anti-cytokine antibody, as set forth on page 5 of the office action mailed on 1/29/2007 and pages 6-7 of the office action mailed on 7/26/2006, is *withdrawn* in response to Applicant's deletion of these terms from the claim.

New grounds of rejection

Claims 54-63 and 65-103 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of transnasal administration of a pharmaceutical composition, wherein said method comprises administering an active ingredient and a carrier comprising a penetrant comprised of a less soluble substance that is a lipid, and a more soluble substance that is a surfactant or a more soluble form of the lipid. The claims do not require the lipids and surfactants of the instant invention to have any feature other than to differ in solubility, nor any particular structure. The specification provides a listing of various lipids and surfactants that are suitable for use in the penetrant of the claimed method. This listing includes phosphatidylcholines as suitable lipids; however, Applicants have disclosed that at least one lipid, didecanoyl-L-alpha-phosphatidylcholine, is not suitable for use in the claimed invention for the reasons discussed *supra*. The specification does not disclose any examples

of lipids or surfactants that are unsuitable, and provides no listing of chemical or physical features that would render a lipid or surfactant unsuitable for use in the claimed method. Thus, the specification does not provide adequate description of the genus of lipids that can be used to create a penetrant with the claimed physical/chemical characteristics.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement that the claimed penetrant comprise a lipid and a surfactant or a more soluble form of the lipid. There is no identification of any specific lipids or surfactants that would not provide the claimed chemical/physical features of the penetrant, nor any physical or chemical features of a lipid or surfactant that must be conserved, or alternatively, excluded, in order to maintain function. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus of lipids and surfactants.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejections withdrawn

1. Rejection of claim 81 under 35 USC § 112, second paragraph, as being indefinite regarding the term "practically sufficient" as set forth on page 6 of the office action mailed on 1/29/2007 and page 9 of the office action mailed on 7/26/2006, is *withdrawn* in response to Applicant's deletion of the term from the claim.

2. Rejection of claim 55 under 35 USC § 112, second paragraph, as being indefinite regarding the term "two forms of a substance" as set forth on page 6 of the office action mailed on 1/29/2007 and page 8 of the office action mailed on 7/26/2006, is *withdrawn* in response to Applicant's amendments to the specification to remove the "etc" from the definition of "two forms of a substance, and thus remove the open-endedness of the definition.

3. Rejection of claim 66 under 35 USC § 112, second paragraph, as being indefinite regarding the term "surfactant-like" as set forth on page 8 of the office action mailed on 1/29/2007 and page 9 of the office action mailed on 7/26/2006, is *withdrawn* in response to Applicant's deletion of the term from the claim.

4. Rejection of claim 64 under 35 USC § 112, second paragraph, is moot in view of Applicant's cancellation of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejections withdrawn

Rejection of claims 54-63 and 65-103 under 35 USC § 103(a) as being obvious in view of the combination of Cevc *et al*, Drejer *et al*, and Hussain *et al*, as set forth on pages 9-10 of the office action mailed on 1/29/2007 and originally set forth on pages 10-12 of the office action mailed on 7/26/2006, is *withdrawn*.

In the response received on 7/26/2007, the Applicants argue that the combination of Cevc, Drejer, and Hussain do not teach or suggest each and every limitation of the instant claims. The Applicants argue that this combination of references teaches away from the instant invention because Drejer teaches that transnasal administration of insulin with the penetration enhancer didecanoyl-L-alpha-phosphatidylcholine resulted in nasal irritation when higher doses were administered and/or with increased number of sprayings. Further, the lipid used in the composition of Drejer, didecanoyl-L-alpha-phosphatidylcholine, would be unsuitable for the method because it is not suitable for use in the claimed penetrant. Specifically, didecanoyl-L-alpha-phosphatidylcholine would not be expected "to form a carrier with a penetrant including layers and aggregates with diameter as claimed (and is expected to instead self-assemble into small aggregates in micellar form)". The Applicants also assert that didecanoyl-L-alpha-phosphatidylcholine used with a surfactant such as Tween 80 "would be unlikely to form a penetrant

composition having layers and aggregates with diameter as claimed (and instead would likely form micelles)". Therefore, one of skill in the art would not find it obvious to use didecanoyl-L-alpha-phosphatidylcholine as the lipid in the claimed penetrant for nasal administration.

Furthermore, the Applicants argue that Cevc teaches *transdermal* administration, rather than the transnasal administration recited in the instant invention. The Applicants assert that Cevc teaches away from the claimed method of transnasal administration because Cevc teaches that transdermal delivery is made feasible by the presence of a transepidermal water activity gradient, which does *not* exist in the strongly hydrated nasal mucosal membranes. In other words, the driving force behind the penetration of lipid vesicles across the skill is created by a difference in water concentration across the skin, which defines a hydration force through which delivery of agents across the skin barrier occurs, and which is not present in transnasal barriers because nasal/transnasal barriers are in a constant state of humidity/hydration.

In the Applicant's declaration by Dr. Gregor Cevc, the Applicants state that the compositions of the instant invention were *unexpectedly* discovered to provide transport across the nasal mucosa despite a high water content on both sides of the mucosal barrier. Thus, the Applicants contend that the disclosure of Cevc, as cited in the obviousness rejection, teaches away from nasal administration, and for these reasons, the claims of the instant invention are not obvious in view of the combination of Cevc, Drejer, and Hussain.

These arguments have been fully considered and are persuasive.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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